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Inverted Sapphyrin: A New Family of Doubly N-Confused Expanded Porphyrins

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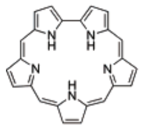
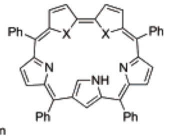
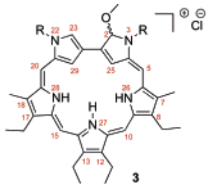
Over the last two decades or so, considerable effort has been devoted to the synthesis of new expanded porphyrins.[1] These quintessential heteroannulenes have been extensively studied as test systems in which issues of aromaticity may be explored. Sapphyrins (e.g., **1**) have attracted particular attention in this regard, with several sapphyrin analogues having been prepared in recent years,[2] including the N-confused core-modified sapphyrins **2**[3] of Furuta and Chandrashekar. In these systems, the N-confused pyrrolic NH is located within the cavity instead of pointing outward as is the case for the corresponding "parent" porphyrin homologues. We now wish to report the synthesis of an inverted sapphyrin derivative **3** where inversion of two pyrrolic nitrogen atoms is configurationally enforced.[4] This system, which, to the best of our knowledge, is the first expanded porphyrin containing a 3,3′-bipyrrolic subunit, displays what is best described as "weak aromaticity" as judged from its spectroscopic features and supporting theoretical calculations.



1a meso-tetraaryl sapphyrin
1b decaalkyl sapphyrin



2 (X = S, Se)

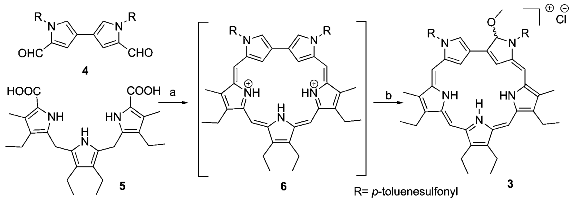


3

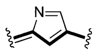
The synthesis of inverted sapphyrin **3** was accomplished via the acid-catalyzed 3+2 condensation between the 3,3′-bipyrrole dialdehyde **4**[5] and the tripyrrane diacid **5**.[6] Although the expected product of this condensation was the sapphyrin-like product **6**, all efforts to isolate this putative intermediate (for which HRMS evidence was obtained) failed; rather, what was obtained in all cases was methanol addition adduct **3**. Presumably, this product arises from the nucleophilic attack of MeOH to one of the tautomers of intermediate **6**.[7] After chromatography on silica gel and treatment with aqueous NH_4Cl, the inverted sapphyrin **3** was obtained in 8−9% yield (Scheme 1).

Inverted sapphyrin **3** is of interest because it displays ^1H NMR spectral features that are consistent with weak aromaticity. For example, the internal β-pyrrolic CH protons are observed as two broad peaks at 3.77 and 4.04 ppm in DMSO-d_6, while the external pyrrolic CH resonance is observed at 8.56 ppm in this same solvent. The chemical shift differences between the internal protons and external protons (4.79 and 4.52 ppm; $\Delta\delta$), generally considered a benchmark of aromaticity, are thus consistent with the presence of a ring current.[8] However, the $\Delta\delta$ values of inverted sapphyrin **3** are considerably less than those seen for typical all-aza *meso*-tetraaryl sapphyrins (e.g., **1a**, average $\Delta\delta$ of 10.97 ppm).[9]

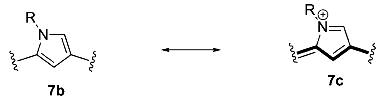
Scheme 1. Synthetic Scheme[a]



[a] Conditions: (a) (i) TFA, CH_2Cl_2, N_2, 12 h; (ii) DDQ, 30 min; (b) (i) silica gel, MeOH; (ii) NH_4Cl (aq).



7a



7b **7c**

The smaller $\Delta\delta$ value observed for **3**, compared to that of the regular sapphyrin **1**, is attributed to the presence of the inverted, N-substituted bipyrrole unit within the macrocycle. Because of this substitution, resonance structures containing uninterrupted 22 π-electron aromatic peripheries can only be written when the charge is present on the inverted, pyrrolic nitrogen (cf. Figure 1). The net consequence of this is that aromaticity is reduced, as it is in most N-substituted N-confused systems reported to date. Whereas in normal, N-confused porphyrins resonance structures containing the imine-like state **7a** can dominate with the consequence that the observed ring current is usually comparable to that seen in the absence of N-confusion,[10] in the case of N-substituted systems containing fragments, such as **7b**, aromatic delocalization is only available through charge-separated resonance contributions (shown in part as structure **7c**). The observed ring currents are thus significantly weaker. Examples of this effect include *N*-methyl N-confused porphyrin,[11] doubly N-confused porphyrin,[12] and the N-confused sapphyrins **2** reported previously, as well as the inverted sapphyrin **3** presented here.[13]

Further support for the proposed weak aromaticity comes from the observed UV−vis spectral features. Whereas the decaalkyl sapphyrin **1b** displays Soret and Q-like bands at 448 and 673 nm when studied as its monoprotonated form in CH_2Cl_2, the UV−vis spectrum of inverted sapphyrin **3** is characterized by features that are shifted to longer wavelengths (λ_{max} (ϵ) = 464 nm (4.45 $\times 10^4$ M^{-1} cm^{-1}) and 827 nm (2.45 $\times 10^4$ M^{-1} cm^{-1})) for the Soret and Q-like bands, respectively (cf. Supporting Information). Interestingly, the extinction coefficient of the Soret band of **3** is only 10% of the value observed for the regular sapphyrin.[14] However, the intensity of Q-like bands is very similar in both compounds.

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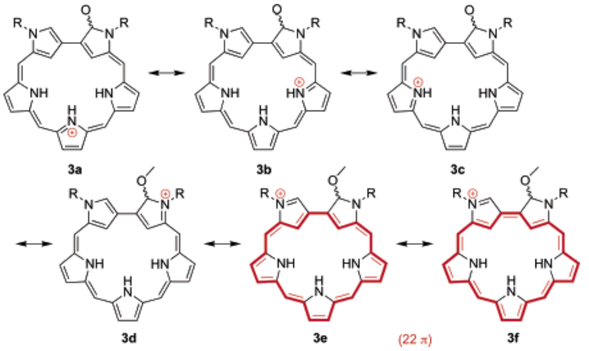

Figure 1. Resonance structures of inverted sapphyrin **3**.

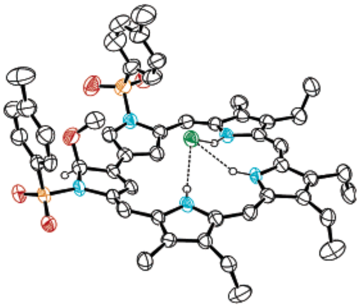

Figure 2. X-ray crystal structure of **3**. Thermal ellipsoids are scaled to the 50% probability level. Most hydrogen atoms and the disorder of one of the *p*-tolyl substituents have been omitted for clarity.

The electronic structure and proposed aromaticity of inverted sapphyrin **3** are consistent with what is predicted by AM1 using the X-ray data of inverted sapphyrin **3**. On the basis of the π orbitals calculated in this way, the HOMO splitting is much smaller than that of the LUMO pair. Using perimeter model terminology, inverted sapphyrin **3** should thus behave as a "negative-hard" chromophore, which is similar to what is seen in the case of isosmaragdyrin, a contracted, aromatic analogue of sapphyrin.[15] For such a chromophore, a large ratio of Q versus Soret type band intensity is predicted, as well as a $-$, $+$, $-$, $+$ sequence of MCD Faraday B terms for the lowest four π−π^* electronic transitions. In fact, the Q/Soret intensity ratio of **3** in the absorption spectrum is similar to that of isosmaragdyrin, while the predicted sequence of B terms is clearly seen in the MCD spectrum of **3** (cf. Supporting Information) for the Soret bands. However, the Q region is somewhat more difficult to interpret, although the overall shape of the spectrum agrees with our expectations. ZINDO/S calculations also predict similar absorption patterns for isosmaragdyrin and inverted sapphyrin **3**. The Q_1 transitions are likewise predicted to be only about 4 times weaker than the Soret bands, and the Q_2 band is predicted to lie closer to the Soret band than Q_1.

The structure of sapphyrin **3** was confirmed by single-crystal X-ray analysis (cf. Figure 2). In analogy to what was seen in the case of a monoprotonated sapphyrin chloride anion salt, the cationic core was found to interact with the chloride counteranion via a set of three pyrrole NH···Cl$^-$ hydrogen bonds. As a consequence, the NH···Cl distances (2.24−2.36 Å) are markedly shorter than the corresponding CH···Cl distances (2.84 and 2.95 Å). Both tosyl substituents, the methoxy group, and the chloride anion lie on the same side of the macrocyclic plane, with the chloride anion lying 1.57 Å above the mean of this plane.

The observed interatomic distances within macrocycle **3** are consistent with a high degree of double bond localization. While the observed bond alternation pattern following approximately that expected for valence structure **3a** (cf. Supporting Information), HOSE calculations (harmonic oscillator stabilization energy)[16] based on the X-ray were used to estimate more precisely the relative importance of canonical structures **3a**−**f** within the overall resonance hybrid. On this basis, it was estimated that the total input of structures **3a**−**d** is 78%, whereas the Kekulé-type structures **3e**−**f** each contribute 11%. This result is in qualitative agreement with the relatively weak aromatic ring current inferred from the ^{1}H NMR spectrum. In addition, the nucleus-independent chemical shift (NICS(0)) values, a widely accepted indicator of aromaticity,[17] were found to be much less negative for inverted sapphyrin **3** (roughly −2.0 ppm) than for sapphyrin **1** (−12 ppm).

In summary, we have demonstrated a new kind of inverted porphyrin analogue that shows spectroscopic properties and structural features that are best considered as being weakly aromatic. This system thus lies along the continuum between highly aromatic expanded porphyrin species, such as sapphyrin, and others that are best considered as nonaromatic or antiaromatic. It is thus likely to be of interest as a probe for methods, both theoretical and experimental, that are currently being developed to explore issues of aromaticity.[18]

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Supporting Information Available: Details describing the synthesis and characterization of compound **3**; details of the HOSE and NICS calculations (PDF), and crystallographic data (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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